REMARKS/ARGUMENTS

Examiner Interview

Applicants thank Examiner Brannock for the courtesy extended to their representative, Melissa E. Kolom, during the telephonic interview held on December 14, 2005. The matters discussed during the interview are substantially as set forth herein.

The Invention

The invention is directed to an isolated or purified human nucleic acid comprising the nucleotide sequence of SEQ ID NO: 1.

The Pending Claims

Claims 3 and 16-18 currently are pending and are directed to the human nucleic acid sequence comprising SEQ ID NO: 1.

The Office Action

The Office Action maintains its rejection of claims 3 and 16-18 under 35 U.S.C. §§ 101 and 112, first paragraph, as allegedly not supported by either a specific and substantial asserted utility or a well-established utility. Reconsideration of these rejections is hereby requested.

Discussion of Rejection Under 35 U.S.C. §§ 101 and 112, First Paragraph

Applicants continue to maintain that the invention defined by the pending claims involves a specific, substantial, and credible utility. In this regard, Applicants have previously indicated that the claimed nucleic acid sequences can be used (a) in a screening or diagnostic method, and (b) for the treatment and/or prophylaxis of cardiovascular disorders, sleep disturbances, disturbances of consciousness, and pain. Applicants also previously demonstrated that the specification of the subject application discloses a reasonable correlation between the activity of the I_h ion channel encoded by the claimed nucleic acid sequence and the asserted utility, and provided documentary evidence supporting this reasonable correlation.

As further evidence of the utility of the claimed invention, and as suggested by the Examiner during the interview conducted on December 14, 2005, Applicants submit herewith documentary evidence that demonstrates a *direct* role for the polypeptide encoded by the claimed nucleic acid sequence in human disease. In this respect, Qu et al., *Circulation, 107*: 1106-1109 (2003), and Plotnikov et al., *Circulation, 109*: 506-512 (2004), disclose that overexpression of hyperpolarization-activated, cyclic nucleotide-gated channel subunit 2 (HCN2) (i.e., the protein encoded by the claimed nucleic acid sequence) functions as a biological pacemaker when delivered via an adenoviral vector to the left atrium of a canine heart. Zicha et al., *Cardiovascular Research, 66*: 472-481(2005), also discloses the use of HCN proteins as biological pacemakers to treat dysrhythmias associated with congestive heart failure (CHF), and suggests the development of therapies that target HCN expression and/or HCN-based currents for the treatment of CHF-related dysrhythmias. In addition, Ludwig et al., *EMBO J., 22*: 216-224 (2003), demonstrates that mice deficient in the HCN2 gene suffer from sinus dysrhythmia, and concludes that defects in HCN2 likely lead to absence epilepsy and sinoatrial node dysfunction in humans.

Thus, the documentary evidence submitted herewith clearly demonstrates a nexus between HCN2 and cardiovascular disease. As such, Applicants have demonstrated that the claimed invention involves a specific, substantial, and credible utility as prescribed in M.P.E.P. § 2107.01. Accordingly, Applicants request the withdrawal of the rejections under Section 101 and 112, first paragraph.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Application No. 09/640,582

Reply to Office Action

Respectfully submitted,

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